What is claimed is:

1. A method of screening a candidate antiviral agent for antiviral activity comprising

(a) preparing a first cell culture comprising cells containing a first subgenomic viral replication system, and a second cell culture comprising cells containing a second subgenomic viral replication system;

(b) adding the candidate antiviral agent to each cell culture;

(c) incubating the cell cultures under conditions and for a time sufficient to detect an antiviral effect by the candidate antiviral agent on the subgenomic viral replication systems; and

(d) determining the effect of the candidate antiviral agent on each viral replication system,

wherein the first subgenomic viral replication system is genetically distinct from the second subgenomic viral replication system.

2. The method of claim 1, wherein the first and second cell cultures are combined before step (b).

3. The method of claim 1, further comprising a cell culture not containing a subgenomic viral replication system.

4. The method of claim 1, wherein at least one of the subgenomic viral replication systems is a replicon.

5. The method of claim 1, wherein at least one of the subgenomic viral replication systems is a defective genome.

6. The method of claim 1, wherein the cells in the first and second cell cultures are mammalian cells and the first and second subgenomic viral replication systems are from mammalian viruses.

7. The method of claim 6, wherein the mammalian cells are human cells and the mammalian viruses are human viruses.

8. The method of claim 7, wherein the human viruses are selected from the group consisting of hepatitis C virus, yellow fever virus, respiratory syncytia virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, adeno-associated virus, Venezuela encephalitis virus, rubella, coxsackivirus, enterovirus, hepatitis A virus, Dengue fever virus, West Nile virus, tick-borne encephalitis virus, astrovirus, rabies virus, influenza virus A, influenza virus B, respiratory syncytial virus, measles, mumps, Ebola virus, Marburg virus, La Crosse virus, California encephalitis virus, Hantaan virus, Crimean-Congo virus, Rift Valley fever, Lassa fever, Argentine hemorrhagic fever virus, Bolivian hemorrhagic fever virus, Colorado tick fever, JC virus, BK virus, herpes simplex virus type two, human cytomegalovirus, varicella-zoster virus, human herpes simplex virus type six, human herpes virus type seven, human herpes virus type eight, human adenovirus, HIV-1, HIV-2, HTLV-1, HTLV-2, and human parvovirus.

9. The method of claim 7, wherein the human viruses are selected from the group consisting of hepatitis C virus, yellow fever virus, respiratory syncytia virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, and adeno-associated virus.

10. The method of claim 7, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus and Sindbis virus.

11. The method of claim 1, wherein the candidate antiviral agent is a chemical that does not comprise an oligopeptide or an oligonucleotide.

12. The method of claim 1, wherein the candidate antiviral agent comprises an oligopeptide or an oligonucleotide.

13. The method of claim 1, wherein the candidate antiviral agent comprises an oligonucleotide or a polynucleotide.

14. The method of claim 1, wherein the candidate antiviral agent comprises a protein.

15. The method of claim 14, wherein the candidate antiviral agent comprises an antibody binding domain.

16. The method of claim 1, wherein the effect of the candidate antiviral agent on at least one of the subgenomic viral replication systems is determined by quantitation of a portion of the nucleic acid of the at least one subgenomic viral replication system.

17. The method of claim 16, wherein the quantitation is performed by nucleic acid amplification.

18. The method of claim 17, wherein the nucleic acid amplification is by RT-PCR.

19. The method of claim 1, wherein the effect of the antiviral agent on at least one of the subgenomic viral replication systems is determined by quantitation of a reporter gene or assayable portion of a fusion protein that is transcribed along with other viral proteins.

20. The method of claim 1, wherein the effect of the antiviral agent on at least one of the subgenomic viral replication systems is determined by quantitation of a viral protein.

21. The method of claim 20, wherein the viral protein is an enzyme and the quantitation is by assay of the activity of the enzyme.

22. The method of claim 1, wherein at least one of the cell cultures comprises cells wherein the subgenomic viral replication system is stably maintained.

23. The method of claim 1, wherein at least one of the cell cultures comprises cells wherein the subgenomic viral replication system is not stably maintained.

24. The method of claim 1, wherein at least one of the cell cultures comprises primary cells.

25. The method of claim 1, wherein the cell cultures are incubated at least 20 h.

26. The method of claim 1, further comprising at least a third cell culture comprising cells containing a third subgenomic viral replication system, wherein the third cell culture is also subjected to steps (a), (b), (c) and (d),

wherein the each subgenomic viral replication system is genetically distinct from every other subgenomic viral replication system.

27. The method of claim 26, wherein all cell cultures comprising a subgenomic viral replication system are combined before step (b).

28. A method of screening a candidate antiviral agent for antiviral activity comprising

(a) combining a first cell culture comprising cells containing a first subgenomic viral replication system and a second cell culture comprising cells containing a second subgenomic viral replication system to make a mixed cell culture;

(b) adding the candidate antiviral agent to the mixed cell culture;

(c) incubating the mixed cell culture under conditions and for a time sufficient to detect an antiviral effect by the candidate antiviral agent on the subgenomic viral replication systems; and

(d) determining the effect of the candidate antiviral agent on each viral replication system,

wherein the first subgenomic viral replication system is genetically distinct from the second subgenomic viral replication system.

29. The method of claim 28, wherein at least one of the subgenomic viral replication systems is a replicon.

30. The method of claim 28, wherein at least one of the subgenomic viral replication systems is a defective genome.

31. The method of claim 28, wherein all of the cells of the mixed cell culture are the same cell line.

32. The method of claim 28, wherein the cells of the mixed cell culture comprise more than one cell line.

33. The method of claim 28, wherein all of the cells in the mixed cell culture are mammalian cells and all of the subgenomic viral replication systems are from mammalian viruses.

34. The method of claim 33, wherein the mammalian cells are human cells and the mammalian viruses are human viruses.

35. The method of claim 34, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, adeno-associated virus, Venezuela encephalitis virus, rubella, coxsackivirus, enterovirus, hepatitis A virus, Dengue fever virus, West Nile virus, tick-borne encephalitis virus, astrovirus, rabies virus, influenza virus A, influenza virus B, respiratory syncytial virus, measles, mumps, Ebola virus, Marburg virus, La Crosse virus, California encephalitis virus, Hantaan virus, Crimean-Congo virus, Rift Valley fever, Lassa fever, Argentine hemorrhagic fever virus, Bolivian hemorrhagic fever virus, Colorado tick fever, JC virus, BK virus, herpes simplex virus type two, human cytomegalovirus, varicella-zoster virus, human herpes simplex virus type six, human herpes virus type seven, human herpes virus type eight, human adenovirus, HIV-1, HIV-2, HTLV-1, HTLV-2, and human parvovirus.

36. The method of claim 34, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, and adeno-associated virus.

37. The method of claim 34, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus and Sindbis virus.

38. The method of claim 28, wherein the candidate antiviral agent is a chemical that does not comprise an oligopeptide or an oligonucleotide.

39. The method of claim 28, wherein the antiviral agent comprises an oligopeptide or an oligonucleotide.

40. The method of claim 28, wherein the candidate antiviral agent comprises an oligonucleotide or a polynucleotide.

41. The method of claim 28, wherein the candidate antiviral agent comprises a protein.

42. The method of claim 41, wherein the candidate antiviral agent comprises an antibody binding domain.

43. The method of claim 28, wherein the effect of the candidate antiviral agent on at least one of the subgenomic viral replication systems is determined by quantitation of a portion of the nucleic acid of the at least one subgenomic viral replication system.

44. The method of claim 43, wherein the quantitation is performed by nucleic acid amplification.

45. The method of claim 44, wherein the nucleic acid amplification is by RT-PCR.

46. The method of claim 28, wherein the effect of the antiviral agent on at least one of the subgenomic viral replication systems is determined by quantitation of a reporter gene or assayable portion of a fusion protein that is transcribed along with other viral proteins.

47. The method of claim 28, wherein the effect of the antiviral agent on at least one of the subgenomic viral replication systems is determined by quantitation of a viral protein.

48. The method of claim 47, wherein the viral protein is an enzyme and the quantitation is by assay of the activity of the enzyme.

49. The method of claim 28, wherein the mixed cell culture comprises cells wherein the subgenomic viral replication system is stably maintained.

50. The method of claim 28, wherein the mixed cell culture comprises cells wherein the subgenomic viral replication system is not stably maintained.

51. The method of claim 28, wherein the mixed cell culture comprises primary cells.

52. The method of claim 28, wherein the mixed cell culture is incubated at least 20 h.

53. The method of claim 28, wherein the mixed cell culture further comprises a third cell culture comprising cells containing a third subgenomic viral replication system.

54. The method of claim 53, wherein the mixed cell culture further comprises a fourth cell culture comprising cells containing a fourth subgenomic viral replication system.

55. A mixed cell culture comprising a first cell culture comprising cells containing a first subgenomic viral replication system and a second cell culture comprising cells containing a second subgenomic viral replication system.

56. The mixed cell culture of claim 55, wherein at least one of the subgenomic viral replication systems is a replicon.

57. The mixed cell culture of claim 55, wherein at least one of the subgenomic viral replication systems is a defective genome.

58. The mixed cell culture of claim 55, wherein all of the cells of the mixed cell culture are the same cell line.

59. The mixed cell culture of claim 55, wherein the cells of the mixed cell culture comprise more than one cell line.

60. The mixed cell culture of claim 55, wherein all of the cells in the mixed cell culture are mammalian cells and all of the subgenomic viral replication systems are from mammalian viruses.

61. The mixed cell culture of claim 60, wherein the mammalian cells are human cells and the mammalian viruses are human viruses.

62. The mixed cell culture of claim 61, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, adeno-associated virus, Venezuela encephalitis virus, rubella, coxsackivirus, enterovirus, hepatitis A virus, Dengue fever virus, West Nile virus, tick-borne encephalitis virus, astrovirus, rabies virus, influenza virus A, influenza virus B, respiratory syncytial virus, measles, mumps, Ebola virus, Marburg virus, La Crosse virus, California encephalitis virus, Hantaan virus, Crimean-Congo virus, Rift Valley fever, Lassa fever, Argentine hemorrhagic fever virus, Bolivian hemorrhagic fever virus, Colorado tick fever, JC virus, BK

virus, herpes simplex virus type two, human cytomegalovirus, varicella-zoster virus, human herpes simplex virus type six, human herpes virus type seven, human herpes virus type eight, human adenovirus, HIV-1, HIV-2, HTLV-1, HTLV-2, and human parvovirus.

63. The mixed cell culture of claim 61, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus, Sindbis virus, poliovirus, Japanese encephalitis virus, hepatits B virus, human papilloma virus, herpes simplex virus type 1, Epstein-Barr virus, and adeno-associated virus.

64. The mixed cell culture of claim 61, wherein the human viruses are selected from the group consisting of hepatitis C virus, respiratory syncytia virus, yellow fever virus and Sindbis virus.

65. The mixed cell culture of claim 55, wherein the mixed cell culture comprises cells wherein the subgenomic viral replication system is stably maintained.

66. The mixed cell culture of claim 55, wherein the mixed cell culture comprises cells wherein the subgenomic viral replication system is not stably maintained.

67. The mixed cell culture of claim 55, wherein the mixed cell culture comprises primary cells.

68. The mixed cell culture of claim 55, further comprising a third cell culture comprising cells containing a third subgenomic viral replication system.

69. The mixed cell culture of claim 68, wherein the mixed cell culture further comprises a fourth cell culture comprising cells containing a fourth subgenomic viral replication system.